Rates and Risk Factors for Unfavorable Outcomes 6 Weeks after Trichiasis Surgery

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Purpose. Several studies of trichiasis recurrence suggest an association between surgical factors and long-term recurrence, yet data on short-term risk factors are limited. This study was conducted to evaluate risk factors for early trichiasis recurrence and other unfavorable short-term outcomes.

Methods. Trichiasis patients presenting for surgery were evaluated for presence of active trachoma and signs of cicatricial outcomes of trachoma, including number of trichiatic lashes, epilation, and entropion. Surgical factors recorded included incision length, surgery duration, and the surgeon performing the operation. Participants were followed up for 6 weeks after surgery and evaluated for eyelid closure defect and trichiasis recurrence; in addition, in two thirds of the patients, eyelid contour abnormality and granuloma formation were evaluated.

Results. First-time trichiasis surgery was performed on 2615 eyelids. Of these, 2601 eyelids without surgical failure were followed up 6 weeks after surgery. Of the eyelids treated, 2.3% had recurrent trichiasis and 1.3% had an eyelid closure defect. Data on eyelid contour abnormalities and granuloma formation were recorded for 1881 eyes, with rates of 1.2% and 10.5%, respectively. Associated risk factors differed by outcome. Surgeon was predictive of eyelid closure defect and granuloma formation. Eyelids with short incisions were nearly four times more likely to have recurrent trichiasis (95% confidence interval, 1.7–9.3). Baseline trichiasis severity was predictive of eyelid contour abnormalities and recurrent trichiasis. Epilation was associated with granuloma formation, but was protective against eyelid closure defect.

Conclusions. Surgical factors are important predictors of unfavorable outcomes in the weeks immediately after surgery. Although the overall rate of serious uncorrectable unfavorable outcomes was very low, the high rate of granuloma formation, which can be treated by removal, highlights the need for follow-up of patients after trichiasis surgery. (ClinicalTrials.gov number, NCT00347776.) (*Invest Ophthalmol Vis Sci.* 2011;52: 2704–2711) DOI:10.1167/iovs.10-5161

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Trachoma remains the leading infectious cause of blindness worldwide, with an estimate of over 1.3 million people blind and 8 million with trichiasis, which puts them at risk of subsequent blindness.[1,2] Repeated episodes of infection with *Chlamydia trachomatis* typically lead to conjunctival scarring. Scarring ultimately can lead to entropion and trichiasis, which may lead to irreversible blindness if not surgically corrected. Previous research has shown that eyes with trichiasis self-reported as being present for more than a year were 4.5 times more likely to have corneal opacity than eyes with incident trichiasis self-reported to have occurred within the past year,[3] highlighting the importance of timely surgical management. Surgical correction of trichiatic lashes is available in many countries. However, several studies have reported trichiasis recurrence rates after surgery ranging from 10% to 42% within 1 year,[4–10] and longer-term recurrence rates are often even higher.[11–16]

Severe trichiasis at baseline has consistently been reported as a risk factor for trichiasis recurrence,[6,9,17,18] and several studies have reported an association between conjunctival inflammation at follow-up and trichiasis recurrence.[6,12,20,21] Investigations into some other risk factors for recurrence remain inconclusive. In a case–control study with 53 cases and 26 controls, Zhang et al.[18] found an association between chlamydial infection and trichiasis recurrence, while in a retrospective cohort study of 394 trichiasis patients, West et al.[12] found no association. Burton et al.[6,19,21] have published multiple articles suggesting an association between bacterial infection and both incident trichiasis and trichiasis recurrence; these studies have not yet been repeated in areas of high trachoma endemicity.

Numerous studies have suggested that trichiasis recurrence after surgery is in part related to surgical skill or performance. A study of trichiasis surgery patients conducted in The Gambia reported that 1-year recurrence rates varied significantly between surgeons (from 0% to 83%).[6] In Tanzania, recurrence rates have varied significantly by district where the surgery was performed.[12] This district-level variation may represent a difference in surgeon-related factors, since in four of the five districts studied, one surgeon in each district conducted most, if not all the surgeries in that district. Furthermore, Merbs et al.[22] demonstrated that left eyelids were significantly more likely to have recurrence than right eyelids (odds ratio [OR], 1.5; 95% confidence interval [CI], 1.0–2.1) and that recurrence was more common on the left side of the eyelid for both right and left eyes. All these studies suggest that recurrence in part may be due to surgical skill and technique, although exactly which aspects of the surgery most influence outcome are unclear. In any case, differences due to surgeon or aspects of the surgery may be evident very early in follow-up, whereas with longer follow-up other host and environmental factors have more time to contribute to unfavorable outcomes.

The Surgery for Trichiasis Antibiotics to prevent Recurrence (STAR) clinical trial was conducted in southern Ethiopia to

examine whether the use of single-dose oral azithromycin at the time of surgery for the patient alone and for the patient plus all household members reduces the risk of trichiasis recurrence within 1 year, compared to 6 weeks of twice daily topical tetracycline, the current standard of care. This study showed a 33% reduction in trichiasis recurrence to 1 year among patients treated with oral azithromycin[9] and followed on the heels of two smaller studies which also evaluated the use of antibiotics at the time of surgery[6,8] but found no association between treatment and overall recurrence at 1 year. Zhang et al.,[8] however, reported a protective effect of azithromycin at one time point, among the subgroup with major trichiasis at baseline. As part of the STAR trial, we evaluated risk factors for early trichiasis recurrence and other unfavorable outcomes of trichiasis surgery 6 weeks after surgery. This time interval was selected because we wanted to evaluate surgical factors during a period when infection was unlikely, because of the antibiotic treatment given at baseline.

METHODS

The STAR clinical trial methods have been described in detail elsewhere.[24] Briefly, patients presenting for first-time trichiasis surgery in the Wolayta Zone, Southern Nations Nationalities and Peoples Region (SNNPR), were invited to participate in the trial. Enrollment occurred during three periods: November through December 2002, March through May 2003, and October through November 2003. Interruptions in enrollment were necessary to ensure that all follow-up visits could occur outside the rainy season, which takes place between June and September. Written informed consent and demographic information were obtained from all patients.

History of previous surgery and self-reported duration of trichiasis were noted. Both eyes of each participant were evaluated for the presence of active trachoma using the WHO simplified grading scheme and characteristics of cicatricial trachoma outcomes, including number and location of lashes touching the globe, number of lashes touching the cornea, evidence of epilation, and degree of entropion. The location of trichiatic lashes was recorded as the nasal, central, and/or temporal one third of the lid, according to the location of the lash base(s). Epilation was recorded as present if one or more empty lash follicles or broken or regrowing lashes were visible. Successful epilation was defined as evidence of epilation without lashes touching the globe. For example, if an individual had evidence of epilation nasally, no lashes touching the globe, and lashes present in the normal position centrally and temporally, the individual was characterized as having successful epilation. Entropion was classified as mild if all lash bases were visible on straight gaze, moderate if some lash bases were visible and others were not, and severe if all lash bases were not visible. For analysis purposes, the mild and moderate categories were combined and compared against the severe entropion category.

Patients were randomly assigned to have surgery performed by one of the Integrated Eye Care Workers (IECWs) specifically certified for this trial.[25] Random assignments to surgeon were created by using a customized program (SAS, Cary, NC) in advance of the trial. Each IECW was assigned a color (blue or pink). Individual forms, prelabeled with the study identification number were printed on either blue or pink paper, according to the IECW assignment for each participant. The IECWs were instructed to operate only on patients with the appropriate color of forms. Adherence to IECW assignment was checked by comparing the IECW's code against the original IECW assignment. In addition, either the project director or the project manager was in the field at all times, monitoring adherence to assignments.

During each of the three surgical periods, two IECWs were assigned primary responsibility for performing the surgeries for the trial. IECW 1 and 2 were responsible for performing surgery during the first two surgical periods. IECW 1 and 3 performed the surgeries during the third period. Two additional IECWs performed a total of 25 surgeries during the study on the 4 days that the assigned IECWs were not available due to illness or other emergencies.

When trichiasis without a history of previous surgery was present bilaterally, one eyelid undergoing surgery was randomly selected to be in the STAR clinical trial; however, surgery was performed on both eyelids and data were recorded for each eyelid. For this article, all eyelids undergoing first-time trichiasis surgery were included in the analysis. When bilateral surgery was performed, the right eyelid was operated first, followed by surgery on the left eyelid. Immediately before surgery, a swab was taken of the upper and lower conjunctiva from the study eye to test for chlamydial infection. Detailed procedures for swab collection, handling, and processing to test for the presence of chlamydial DNA are provided elsewhere.[24] Briefly, swabs were collected according to standard procedures to prevent contamination and then were stored frozen until they were shipped to the Johns Hopkins International Chlamydia laboratory where they were processed for presence of chlamydial DNA. The bilamellar tarsal rotation (BLTR) procedure was performed for all eyelids undergoing surgery.[7]

Surgical data collected included the amount of local anesthesia given, duration of surgery (in minutes) and length of the incision (in millimeters). The incision length was determined by cutting a piece of suture material that extended from one end of the incision to the other, following the contour of the eyelid. The suture material was then measured with a ruler marked in millimeter increments. Standardization testing of 20 eyelids showed that when two separate pieces of suture material were measured for the same incision by the same surgeon, the measured incision lengths varied by less than 0.5 mm. Short incisions were defined as incisions that fell within the 5% tail of the distribution of all incisions ($<$22 mm). After surgery, all patients were treated with topical tetracycline or oral azithromycin, according to the STAR trial protocol treatment group assignments. One third of participants received topical tetracycline twice daily for 6 weeks and two thirds received a single 1-g dose of oral azithromycin on the day of surgery.

Sutures were removed 2 weeks after surgery by an IECW who was not present at the time of surgery. Follow-up visits were conducted by IECWs not involved in the trichiasis surgery. All four IECWs involved in the 6-week follow-up data collection were standardized for trichiasis grading against a senior trichiasis grader. Agreement (κ) on trichiasis grading was above 0.7 for all graders. At the 2-week follow-up visit, surgical failure was defined as the presence of one or more lashes touching the globe. Patients were re-examined at 6 weeks after surgery.

At the 6-week visit, data collected included swabs to test for chlamydial infection, trichiasis recurrence (the presence of one or more lashes touching the globe and/or evidence of epilation confirmed by questioning the patient), and the presence of an eyelid closure defect (a gap between the eyelids through which the globe was visible when the eyelids were closed). During the first surgical period, the follow-up IECW noted several eyelids with a distorted contour that did not result in an eyelid closure defect (Fig. 1A), which we have defined as *eyelid contour abnormality*, as well as several inflammatory masses, or *pyogenic granulomas*, of the upper tarsal conjunctiva (Fig. 1B). Therefore, the presence of an eyelid contour abnormality and/or a pyogenic granuloma was systematically recorded at the 6-week visit during the second and third follow-up periods.

Bivariate associations between potential risk factors, such as patient demographics and preoperative eyelid characteristics, and outcomes were analyzed by using logistic regression models that accounted for the correlation between eyes of the same subject (procedure GENMOD with exchangeable correlation structure); odds ratios and 95% confidence intervals are presented (SAS, ver. 9.1). Multivariate models to examine independent contributions of potential risk factors were constructed in a similar approach; all models were adjusted for age and sex. Contingency tables were used to examine the associations between outcomes.

All study procedures were approved by the Johns Hopkins Medicine Institutional Review Board and the Ethiopia Science and Technol-

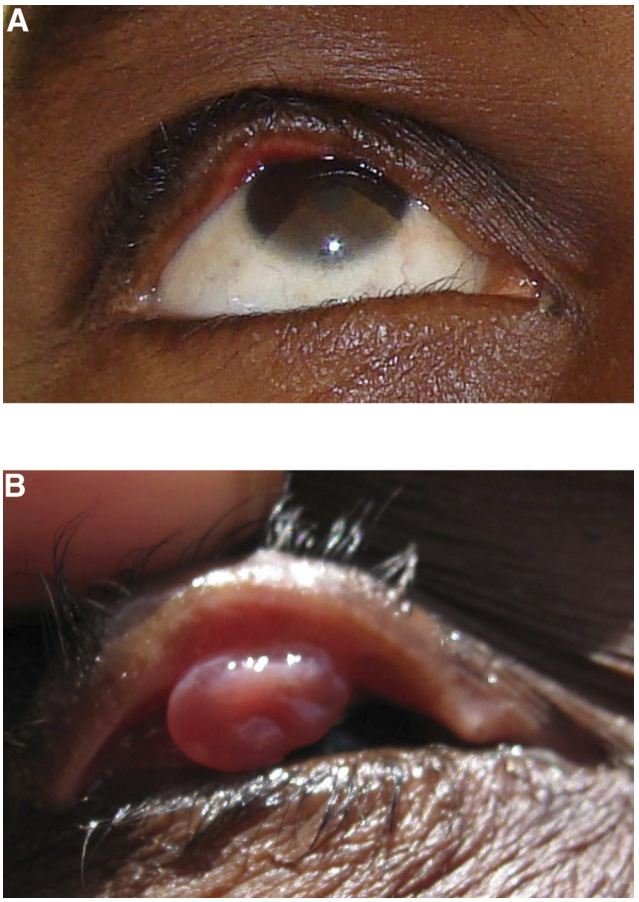

FIGURE 1. Lid contour abnormality (**A**) and pyogenic granuloma (**B**) after trichiasis surgery.

ogy Commission. The study complied with the tenets of the Declaration of Helsinki.

RESULTS

A total of 1452 individuals were enrolled in the STAR trial, and each participant had either unilateral or bilateral surgery performed, as needed. Among these individuals, 2615 eyelids underwent first-time trichiasis surgery. One unilateral surgery participant and four bilateral surgery participants were not followed up at 6 weeks after surgery. Baseline characteristics of the study sample are summarized in Table 1 and are reported in detail elsewhere.[3] Seventy-seven percent of the participants were female, and 80% had bilateral trichiasis. Severe trichiasis was common in this population. Of all the eyelids, 1256 (48%) of eyelids had at least five lashes touching the globe, nearly 70% had evidence of epilation and 46% had moderate or severe entropion.

At baseline, 19% of participants had ocular chlamydial infection. At the 6-week visit, the rate of chlamydial infection dropped to 1.9% (49 eyes of 27 people). As expected, infection at 6 weeks was more common among participants in the tetracycline arm than in the azithromycin arm (4.2% vs. 0.7%, $P < 0.01$). However, no statistically significant differences in 6-week event rates were seen across the three treatment groups; therefore, no adjustment was made for treatment group in subsequent analyses. At the 2-week follow-up visit, five surgically treated eyelids had lashes touching the globe. These eyelids were more likely to have severe baseline trichiasis, active trachoma at the time of surgery, and a longer duration of surgery. Surgery was considered an immediate failure in these patients, and they were not included in any further analyses for this article.

Trichiasis Recurrence

At the 6-week follow-up visit, 59 eyelids had recurrence (Table 2). Not surprisingly, two markers of preoperative trichiasis severity were predictive of recurrent trichiasis. Eyelids with nine or more lashes touching the cornea before surgery were 2.6 times more likely (95% CI, 1.4–4.8) to have recurrence than eyelids with one to four lashes touching before surgery; likewise, eyelids with trichiatic lashes in three locations at baseline were more likely to have recurrence than eyelids with trichiatic lashes in one location at baseline (OR, 2.2; 95% CI, 1.2–4.4). Although the table suggests that having five to eight lashes touching the cornea was protective against recurrence, this finding represents only one eyelid with recurrence, making it impossible to draw conclusions from the results in this small subgroup. Of all the eyes, 1.9% had ocular chlamydial infection at follow-up. Chlamydial infection at follow-up was more common in eyes with recurrence (5.1% vs. 1.9%; Fisher's exact $P = 0.09$); however, the limited number of events restricted the power to fully examine this comparison.

The sex of the individual and baseline chlamydial infection were not associated with recurrent trichiasis; however, there was a nonstatistically significant trend for age. Older individuals tended to have trichiasis recurrence more often than younger individuals, with a 20% increased risk of recurrence for every 10-year increase in age. The duration of surgery was not associated with recurrent trichiasis, and no difference in trichiasis recurrence rates was seen between IECWs. The mean incision length was 26.1-mm (range, 18–37 mm). Eyelids with recurrent trichiasis were 3.6 times more likely to have a short incision (<22 mm; 95% CI, 1.3–9.2). In multivariate analyses, severe trichiasis at baseline and length of incision remained predictive of trichiasis recurrence to the same degree reported in bivariate analyses.

Eyelid Closure Defect

Eyelid closure defects were present at 6 weeks in 35 (1.3%) surgically treated eyelids. Statistically significant differences were seen in the frequency of eyelid closure defects between IECWs ($P = 0.004$); IECW 2 had the highest rate (2.1%), whereas IECW 3 had no eyelid closure defects (Table 2). Interestingly, eyelids with evidence of epilation at baseline

TABLE 1. Characteristics of the 1452 Participants

Characteristic	*n*	%
Age Group, y		
<30	105	7.2
30–39	253	17.4
40–49	336	23.1
50–59	384	26.4
≥60	374	25.8
Sex		
Male	331	22.8
Female	1121	77.2
Treatment		
Azithromycin	968	66.7
Tetracycline	484	33.3
Trichiasis surgery		
Unilateral	278	19.2
Bilateral	1174	80.2
Ocular chlamydia infection		
No	1172	80.7
Yes	280	19.3

TABLE 2. Factors Associated with Trichiasis Recurrence and Eyelid Closure Defect: Eyes from All Surgical Periods

Characteristic	Number of Surgeries	Trichiasis between 2 and 6 Weeks		Eyelid Closure Defect	
		%	Crude OR* (95% CI)	%	Crude OR* (95% CI)
Overall	2601	2.27		1.35	
Age group, y					
<30	190	1.58	1.19 (0.96–1.47) per 10-y increase in age	0.53	1.17 (0.89–1.53) per 10-y increase in age
30–39	451	2.22		0.89	
40–49	596	2.01		1.34	
50–59	693	2.45		1.73	
≥60	671	2.68		1.49	
Sex					
Male	577	2.25	1.00	1.73	1.00
Female	2024	2.27	1.01 (0.53–1.90)	1.24	0.71 (0.29–1.72)
Baseline Trichiasis Characteristics					
Baseline ocular chlamydia infection					
No	2097	2.43	1.00	1.53	1.00
Yes	504	1.59	0.65 (0.28–1.48)	0.60	0.39 (0.08–1.78)
Baseline active trachoma (TF +/− TI)					
No	1932	1.97	1.00	1.19	1.00
Yes	664	3.16	1.63 (0.90–2.94)	1.81	1.53 (0.68–3.44)
Evidence of epilation					
No	800	1.63	1.00	2.25	1.00
Yes	1801	2.55	1.59 (0.82–3.08)	0.94	**0.41 (0.19–0.91)**
Number of lashes touching the globe					
None (epilating only)	610	2.46	1.65 (0.74–3.67)	0.98	0.65 (0.22–1.87)
1–4	733	1.50	1.00	1.50	1.00
5–9	520	1.73	1.15 (0.48–2.80)	1.73	1.15 (0.48–2.76)
>9	736	3.26	**2.20 (1.05–4.59)**	1.22	0.81 (0.29–2.23)
Number of lashes touching the cornea					
None (epilating only)	780	2.30	1.07 (0.55–2.08)	1.03	0.75 (0.28–2.04)
1–4	1030	2.23	1.00	1.36	1.00
5–8	373	0.27	**0.13 (0.02–0.96)**	1.88	1.39 (0.54–3.54)
≥9	413	4.83	**2.56 (1.37–4.77)**	1.45	1.07 (0.38–3.01)
Number of locations with trichiatic lashes†					
None (epilating only)	610	2.46	1.51 (0.70–3.26)	0.98	0.51 (0.20–1.32)
1	793	1.64	1.00	1.89	1.00
2	497	1.21	0.73 (0.28–1.94)	1.41	0.74 (0.28–1.99)
3	694	3.60	**2.24 (1.15–4.36)**	1.01	0.53 (0.19–1.48)
Severe entropion					
No	2182	2.06	1.00	1.33	1.00
Yes	418	3.35	1.65 (0.90–3.02)	1.44	1.08 (0.39–2.97)
Surgery Characteristics					
Surgical eyelid					
Right	1291	2.32	1.00	1.55	1.00
Left	1310	2.21	0.95 (0.59–1.54)	1.15	0.74 (0.46–1.18)
IECW performing surgery					
1	1286	1.94	0.84 (0.38–1.83)	1.24	
2	901	2.66	1.16 (0.53–2.54)	2.11	***P* = 0.003**‡
3	389	2.31	1.00	0.00	
4‡	23	4.35	—	0.00	
5‡	2	0.0	—	0.00	
Duration of surgery (min)					
<10	139	2.88	1.27 (0.44–3.66)	1.44	
10–14	1539	2.27	1.00	1.30	1.00
15–19	786	2.16	0.95 (0.52–1.74)	1.27	
≥20	137	2.19	0.96 (0.29–3.19)	2.19	1.70 (0.50–5.80)
Length of incision (mm)					
<22	69	8.25	**3.58 (1.39–9.23)**	1.45	1.08 (0.14–8.15)
≥22	2532	2.13	1.00	1.34	1.00
Postsurgical treatment					
Azithromycin	1731	1.91	0.63 (0.36–1.10)	1.44	1.26 (0.50–3.17)
Tetracycline	870	2.99	1.00	1.15	1.00

Bold data represent statistically significant results.

* Adjusted for the correlation between eyelids.

† Based on nasal, central and temporal lashes. Eyelids classified as "none" were those eyelids which were epilated and had no other trichiatic lashes.

‡ Fisher's exact test. IECWs 4 and 5 served as substitutes for the 3 days when one regularly scheduled IECW was unavailable during the first surgical period. They are excluded from the Fisher's exact test because of the very low volume of surgeries performed (25 cases total).

were less likely to have eyelid closure defects at follow up than were eyelids with lashes touching the globe and no evidence of epilation (OR, 0.4; 95% CI, 0.2–0.9) at baseline. The rate of eyelid closure defects also showed a nonsignificant increase with increasing age. None of the baseline trichiasis severity measures were predictive of an eyelid closure defect at 6 weeks. Given the limited number of eyelid closure defects, multivariate analyses were not performed.

Eyelid Contour Abnormality

Eyelid contour abnormalities and granuloma formation were systematically recorded during the second and third enrollment periods. Among the 1881 eyelids that underwent surgery during these two periods, 22 (1.2%) had evidence of lid contour abnormality at follow-up (Table 3). The rate of lid contour abnormality did not differ significantly across IECWs, with all IECWs having contour abnormality frequencies of less than 2%. Factors associated with contour abnormality included older age and baseline trichiasis severity; eyelids with nine or more lashes touching the cornea at baseline were 4.3 times more likely to have an eyelid contour abnormality than eyelids with one to four lashes touching the cornea (95% CI, 1.4–13.1). In multivariate analyses, these factors remained predictive of eyelid contour abnormality, with significance of the same magnitude and direction.

Pyogenic Granuloma Formation

Pyogenic granuloma formation occurred after 198 of 1881 surgeries (10.5%). Females were significantly less likely to develop granulomas than were males (OR, 0.51; 95% CI, 0.35–0.74; Table 3). Furthermore, eyelids that were successfully epilated (i.e., had no locations involved because all trichiatic lashes were epilated) were 55% more likely to have a granuloma than eyelids that had at least one lash touching the globe at baseline (95% CI, 1.1–2.2). Granulomas occurred nearly twice as often after surgery performed by IECW 1 compared with surgeries performed by IECW 2 and 3 (14% vs. 7% and 8%, respectively). Similar to other outcomes, factors that were predictive in bivariate models remained predictive to the same degree and magnitude in multivariate analyses.

A summary of the statistically significant associations between risk factors and each outcome is provided in Table 4.

Correlation between Outcomes

Eyes with trichiasis recurrence had a significantly higher rate of eyelid closure defect (5.1% vs. 1.3%; Fisher's exact test $P = 0.043$) and lower rates of granuloma formation (4.7% vs. 10.7%, Fisher's exact test $P = 0.31$) than eyes without recurrence (Table 5). Power to examine the correlation between granuloma and recurrence was limited, since only 43 eyes had recurrence during the timeframe in which granuloma formation was assessed. No other correlations between outcomes were substantively different.

Discussion

In this study, the rate of unfavorable outcomes by 6 weeks after surgery, excluding the formation of pyogenic granulomas that are resectable, was extremely low, totaling less than 5%. Granulomas were identified in slightly more than 10% of surgically treated eyelids. All granulomas were excised at the 6-week visit. For each unfavorable outcome, the risk factors associated with the outcome differed. These differences are not surprising, given the inherent differences in the outcomes themselves.

Trichiasis Recurrence

Early trichiasis recurrence in this study was uncommon; less than 3% of patients had evidence of trichiasis recurrence 6 weeks after surgery. In contrast, a previous study conducted in Egypt reported a recurrence rate of 16% at 8 weeks after surgery.[26] Preoperative trichiasis severity has consistently been associated with trichiasis recurrence in long-term follow-up studies.[6,9,17,18] Similarly, in this study, increased baseline severity was associated with increased risk of trichiasis recurrence at 6 weeks after surgery. This finding probably is a result of the severe thickening and vertical and horizontal shortening of the eyelid before surgery, which makes eyelid eversion more difficult. Furthermore, individuals with severe incident trichiasis could also have an unidentified genetic predisposition to severe trichiasis or shorter eyelid dimensions that would make them more susceptible to trichiasis recurrence. Recently, some researchers have begun to focus attention on the genetic aspects of trachomatous scarring, trichiasis, and trichiasis recurrence,[27–29] and these studies suggest that indeed some genetic predispositions may exist. Alternatively, individuals with severe incident trichiasis and trichiasis recurrence may be exposed to environmental factors that have not been clearly identified as risk factors for trichiasis and therefore were not reported in this study.

Of interest, to our knowledge, this study is the first to report an association between decreased incision length and increased risk of trichiasis recurrence, even after adjustment for baseline trichiasis severity. Eyelids in which the incision was <22 mm long had nearly a fourfold increased frequency of trichiasis recurrence compared with eyelids with longer incisions. A short incision may prohibit adequate rotation of the distal fragment in the nasal and temporal regions, resulting in undercorrection in these segments of the eyelid. Indeed, all eyelids with short incisions and recurrence had temporal and/or nasal recurrence. Alternatively, eyes with shorter incisions may have smaller dimensions, which may pose a greater surgical challenge, since they are more difficult to evert. In this study, we did not measure length of the eyelid, so we were not able to examine this possibility.

Eyelid Closure Defect

Eyelid closure defect was also rare, occurring after approximately 1.5% of all surgeries. Both incorrect placement of the incision and the overtightening of sutures can lead to an eyelid closure defect, so it is not surprising that rates of eyelid closure defect varied significantly across surgeons (range, 0%–2.1%). Interestingly, evidence of epilation had a decreased risk of eyelid closure defect. It is unclear why the physical act of removing eyelashes would make contour defects less likely after surgery. We cannot rule out the possibility that this association was found by chance, since we evaluated multiple outcomes and multiple risk factors. Although the same follow-up examiner performed all follow-up visits within a surgical period, multiple follow-up examiners were used during the course of the study, and we cannot rule out slightly differential grading across examiners.

Pyogenic Granuloma

Granuloma was the most frequently observed outcome at 6 weeks, with 10.5% of eyelids having granulomas present. Conjunctival pyogenic granulomas are polypoid and friable capillary hemangiomas, which are inflammatory lesions typically found in association with chalazia or after ocular or eyelid surgery.[29] We found that surgeons had different rates of granuloma formation after surgery. This finding is not surprising, given that granulomas can form as a result of rough edges from

TABLE 3. Baseline Trichiasis and Surgical Factors Associated with Presence of Eyelid Contour Abnormality and Granuloma 6 Weeks after Surgery from the Second and Third Surgical Periods Only

		Eyelid Contour Abnormality		Pyogenic Granuloma	
Characteristic	**Surgeries (*n*)**	**%**	**Crude OR* (95% CI)**	**%**	**Crude OR* (95% CI)**
Overall	1881	1.17		10.53	
Age group, y					
<30	137	0.00	1.75 (1.24–2.48) per 10-y increase in age	16.06	0.89 (0.78–1.03) per 10-y increase in age
30–39	337	0.30		10.09	
40–49	397	0.50		12.09	
50–59	506	1.58		9.29	
≥60	504	2.18		9.33	
Sex					
Male	406	1.97	1.00	16.26	1.00
Female	1475	0.95	0.48 (0.17–1.32)	8.95	**0.51 (0.35–0.74)**
Baseline Trichiasis Characteristics					
Baseline ocular chlamydial infection					
No	1540	1.10	1.00	10.65	1.00
Yes	341	1.47	1.33 (0.41–4.39)	9.97	0.93 (0.60–1.45)
Baseline active trachoma (TF +/− TI)					
No	1437	1.18		10.79	1.00
Yes	443	1.13	0.95 (0.37–2.46)	9.71	0.95 (0.37–2.46)
Evidence of epilation					
No	631	1.74	1.00	9.19	1.00
Yes	1250	0.88	0.50 (0.18–1.37)	11.20	1.25 (0.88–1.76)
Number of lashes touching the cornea					
None (epilating only)	523	0.96	1.50 (0.43–5.22)	13.00	1.33 (0.93–1.92)
1–4	784	0.64	1.00	10.08	1.00
5–8	273	1.47	2.32 (0.62–8.69)	6.59	0.63 (0.37–1.06)
≥9	300	2.67	**4.27 (1.39–13.1)**	10.67	1.07 (0.66–1.72)
Number of locations involved†					
None	413	1.21	1.26 (0.38–4.26)	14.04	**1.55 (1.09–2.21)**
1	625	0.96	1.00	9.28	1.00
2	367	1.36	1.42 (0.42–4.79)	10.63	
3	475	1.26	1.32 (0.42–4.11)	9.05	
Severe entropion					
No	1614	1.30	1.00	10.41	1.00
Yes	267	0.37	0.29 (0.04–2.18)	11.24	1.09 (0.69–1.73)
Surgery Characteristics					
Surgical eyelid					
Right	930	1.08	1.00	11.40	1.00
Left	951	1.26	1.18 (0.63–2.20)	9.67	0.83 (0.65–1.06)
IECW performing surgery					
1	945	1.59	3.12 (0.68–14.3)	14.0	**2.27 (1.33–3.85)**
2	542	0.92	1.80 (0.32–10.2)	7.38	1.11 (0.60–2.05)
3	389	0.51	1.00	6.68	1.00
Duration of surgery (min)					
<10	114	0.88	0.77 (0.10–6.07)	12.28	0.98 (0.94–1.04) per 1 minute increase
10–14	1141	1.14	1.00	10.69	
15–19	522	1.34	1.18 (0.38–3.63)	10.15	
≥20	104	0.96	0.84 (0.12–5.74)	8.65	
Length of incision (mm)					
<22	38	0.0	Fisher's exact	10.53	1.00 (0.34–2.90)
≥22	1843	1.19	$P = 0.63$	10.53	1.00
Postsurgical treatment					
Azithromycin	1252	1.60	5.09 (0.67–38.8)	10.70	1.06 (0.74–1.52)
Tetracycline	629	0.32	1.00	10.17	1.00

Bold data represent statistically significant results.

* Adjusted for the correlation between eyelids

† Based on nasal, central and temporal lashes. Eyelids classified as "none" were those eyelids which were epilated and had no other trichiatic lashes.

foreign bodies, like sutures, or from chalazia. BLTR is particularly susceptible to the creation of jagged tarsal edges because the full-thickness eyelid incision must be made in four steps: first incising the skin and orbicularis, next everting the eyelid, then incising the conjunctiva and tarsus to join with the skin incision, and finally extending the incision both nasally and temporally with scissors. Interestingly, successful epilation (removal of all trichiatic lashes), was predictive of increased risk of granuloma formation, perhaps because it is more difficult to determine where to make the corresponding skin incision

TABLE 4. Summary of Factors Associated with Each Unfavorable Outcome

	Trichiasis Recurrence	Eyelid Closure Defect	Eyelid Contour Abnormality	Pyogenic Granuloma
n	59	35	22	198
Age	Borderline association, older age increased risk		1.75 Increase in risk per 10-y increase in age	
Sex				Being female decreased risk
Baseline trichiasis severity	9+ Lashes touching cornea increased risk		9+ Lashes touching cornea increased risk	
Locations with trichiatic lashes at baseline, *n*	3 Locations increased risk			
Length of incision	Shorter length increased risk			
Evidence of epilation		Any evidence of epilation was protective		Complete epilation increased risk
Eye care worker		IECW 2 had highest, IECW 3 had none		IECW 1 had highest rate (14%); IECW 3 had lowest (6.7%)

when one of the natural guides for measuring the incision (lashes) is absent.

Another possible cause of granulomas in our study was a small piece of suture material left in the eyelid when the sutures were removed. In our study, a single person not involved with the surgery was responsible for removing all sutures during a given surgery period, and the rate of granuloma formation did not differ significantly by surgical period. Although this finding may suggest that suture material remaining within the wound is unlikely to explain the difference in granuloma rate across surgeons, it is also quite possible that the surgeons with higher rates of granuloma formation tied tighter sutures, making them more difficult to remove completely.

We found an inverse correlation between older age and granuloma formation. One study of 100 granulomas in patients ranging in age from 2 to 91 found a mean age of 34 years (less than the median of 45) suggesting that pyogenic granulomas are more common in younger patients. In a discussion that accompanied that paper, a review of the last 60 cases from the University of Cincinnati also found a mean age of 36 years (range 4–86).[30] Because very little has been published about conjunctival pyogenic granulomas, we reviewed our own experience (an academic oculoplastic service) and found that within a 10-year period the mean age of 62 consecutive patients with the diagnosis of pyogenic granuloma was younger than the mean age of the last 200 consecutive patients seen for any reason (46 years vs. 54 years; $P = 0.03$). In our present study, females were nearly 50% less likely to develop granulomas after BLTR than males. Although in the published study mentioned earlier, an equal number of male and female patients with granulomas were found,[30] 23 of the 60 patients from the University of Cincinnati were female and 27 of our own 62 patients with granulomas were female, consistent with the results of our present study. Whether this disparity is related to hormonal or behavioral differences is unclear.

Eyelid Contour Abnormality

Older age was predictive of increased eyelid contour abnormalities and eyelid closure defect. Older eyelids have increased horizontal length and laxity,[31] making them less stable. A floppy eyelid is more difficult to rotate and evenly fixate, which is one explanation for the association between contour abnormalities and closure defects and age. Alternatively, older age may be a marker of more severely scarred eyelids, which are stiff and more difficult to uniformly rotate. Although these models are adjusted to account for baseline trichiasis severity, the measure of baseline severity used—the number of trichiatic lashes—may not fully capture the degree of conjunctival scarring.

Limitations

As with all studies, this one has limitations. While a tribute to the surgeons in this study, the low rate of unfavorable outcomes limited our ability to evaluate some associations. Specifically, we could not fully evaluate interactions between outcomes. In addition, the role of surgical factors is likely to be more significant in settings where trichiasis recurrence rates are high. Furthermore, during the course of the study, four eye care workers participated in follow-up visits. Because these individuals worked sequentially, we could not evaluate the agreement across each of the evaluators. However, we feel that large differences across graders are unlikely, since each exam-

TABLE 5. Correlation between Outcomes

	Surgeries (*n*)	Closure Defect (%)	Surgeries (*n*)	Pyogenic Granuloma (%)	Contour Abnormality (%)
Recurrent trichiasis					
No	2542	1.3*	1838	10.7	1.2
Yes	59	5.1*	43	4.7	0
Closure defect					
No			1856	10.6	1.3
Yes			25	8.0	0
Pyogenic granuloma					
No			1683	—	1.2
Yes			198	—	1.0

* Fisher's exact test 0.043.

iner was standardized against our gold-standard grader before working independently.

Conclusions

The results of this study suggest that high-quality surgery with a low rate of unfavorable outcomes is attainable. In this study, all individuals performing surgery underwent certification by a highly skilled ophthalmologist who followed the WHO final trichiasis surgical assessment procedures,[25] and the low rate of unfavorable outcomes suggests that this certification may be beneficial in identifying highly skilled surgeons. Even within this group of well-trained eye care workers, however, additional observation and training may help to further improve outcomes. In particular, research into granuloma formation, focused on observing surgical technique, may help to reduce the rate of this complication. Furthermore, investigation into new surgical techniques or new instrumentation that would eliminate the need to evert the lid during surgery should be considered. If the full-thickness incision could be made with a single scalpel blade cut, the tarsal edges of the incision might be more likely to be smooth and not jagged, and therefore may be less likely to incite granuloma formation. Also, eliminating the need to evert the eyelid could allow longer incisions to be made for eyelids with shorter palpebral widths and may reduce recurrence. Regardless of improvements that could be made, these results highlight the importance of follow-up of all trichiasis patients periodically after surgery to excise granulomas and optimize surgical outcomes.

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